## Prior Authorization Review Panel

**CHC-MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

| | |
|---|---|
| **Plan: PA Health & Wellness** | **Submission Date: 09/01/2022** |
| **Policy Number: PA.CP.PHAR.417** | **Effective Date: 01/2020**<br>**Revision Date: 08/2022** |
| **Policy Name: Brexanolone (Zulresso)** | |

**Type of Submission – Check all that apply:**

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

**Please provide any changes or clarifying information for the policy below:**

per updated prescribing information, updated indication and age requirements from adults (18 years) to 15 years of age or older.

| | |
|---|---|
| **Name of Authorized Individual (Please type or print):**<br><br>**Venkateswara R. Davuluri, MD** | **Signature of Authorized Individual:** |

# Clinical Policy: Brexanolone (Zulresso)

Reference Number: PA.CP.PHAR.417
Effective Date: 01/2020
Last Review Date: 08/2022

Coding Implications
Revision Log

**Description**
Brexanolone (Zulresso™) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator.

**FDA Approved Indication(s)**
Zulresso is indicated for the treatment of postpartum depression (PPD) in patients 15 years and older.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness® that Zulresso is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Postpartum Depression** (must meet all)**:**

1. Diagnosis of a major depressive episode that began no earlier than the third trimester and no later than the first 12 weeks following delivery, as diagnosed by Structured Clinical Interview for DSM-5;
2. Prescribed by or in consultation with psychiatrist;
3. Age ≥ 15 years;
4. Member meets one of the following (a, b, c, or d):
   a. HAMD score is ≥ 17 (moderate to severe depression) (*see Appendix D*);
   b. MADRS score is ≥ 20 (moderate to severe depression) (*see Appendix D*);
   c. PHQ-9 score is ≥ 15 (moderate to severe depression) (*see Appendix D*);
   d. Failure of an 8-week trial of one of the following oral antidepressants at up to maximally indicated dose but no less than the commonly recognized minimum therapeutic dose, unless clinically significant adverse effects are experienced or all are contraindicated: selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI), tricyclic antidepressant (TCA), bupropion, mirtazapine (*see Appendix B*);
5. No more than 12 months have passed since member has given birth;
6. Dose does not exceed 90 mcg/kg per hour over 60 hours (2.5 days) as follows:
   a. 0 to 4 hours: Initiate with a dosage of 30 mcg/kg per hour;
   b. 4 to 24 hours: Increase dosage to 60 mcg/kg per hour;
   c. 24 to 52 hours: Increase dosage to 90 mcg/kg per hour (alternatively consider a dosage of 60 mcg/kg per hour for those who do not tolerate 90 mcg/kg per hour);
   d. 52 to 56 hours: Decrease dosage to 60 mcg/kg per hour;
   e. 56 to 60 hours: Decrease dosage to 30 mcg/kg per hour.

**Approval duration: 30 days (one time infusion per pregnancy)**

**B. Other diagnoses/indications**
1. Refer to PA.CP.PMN.53

## II. Continued Therapy

**A. Postpartum Depression**
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

**Approval duration: Not applicable**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration
HAM-D: Hamilton Rating Scale for Depression
MADRS: Montgomery-Åsberg Depression Rating Scale
PHQ-9: Patient Health Questionnaire
PPD: postpartum depression
SNRI: serotonin-norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant

*Appendix B: Therapeutic Alternatives*
*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| ***SSRI*** | | |
| citalopram (Celexa®) | 20 mg PO QD; may increase to 40 mg PO QD after one week | 40 mg/day (≤ 60 years)<br>20 mg/day (> 60 years) |
| escitalopram (Lexapro®) | 10 mg PO QD; may increase to 20 mg PO QD after 1 week | 20 mg/day |
| fluoxetine (Prozac®, Prozac Weekly®) | Prozac: 20 mg PO QD; may increase by 10-20 mg after several weeks<br><br>Prozac Weekly: 90 mg PO q week beginning 7 days after the last daily dose | Prozac: 80 mg/day<br><br>Prozac Weekly: 90 mg/week |
| paroxetine (Paxil®, Paxil CR®, Pexeva®) | Paxil, Pexeva: 20 mg PO QD; may increase by 10 mg every week as needed<br><br>Paxil CR: 25 mg PO QD; may increase by 12.5 mg every week as needed | Paxil, Pexeva: 50 mg/day<br><br>Paxil CR: 62.5 mg/day |
| sertraline (Zoloft®) | 50 mg PO QD; may increase every week as needed | 200 mg/day |
| ***SNRIs*** | | |
| duloxetine (Cymbalta®) | 20 mg PO BID or 30 mg PO BID or 60 mg PO QD | 120 mg/day |
| venlafaxine (Effexor®, Effexor XR®) | Effexor: initial dosing = 37.5-75 mg/day. Doses >37.5 mg administered in 2-3 divided doses; may increase by 75 mg every 4 days as needed<br><br>Effexor XR: 75 mg PO QD; may increase by 75 mg every 4 days as needed | Effexor: 225 mg/day (outpatient) or 375 mg/day (inpatient)<br><br>Effexor XR: 225 mg/day |
| desvenlafaxine (Pristiq®, Khedezla®) | 50 mg PO QD | 400 mg/day |
| Fetzima® (levomilnacipran) | 20 mg PO QD for 2 days, then 40 mg PO QD; may increase by 40 mg every 2 days | 120 mg/day |
| ***TCAs*** | | |
| amitriptyline (Elavil®) | 25 to 50 mg/day PO QD or divided doses | *150 mg/day* |
| amoxapine | 25 to 300 mg/day PO in divided doses | *400 mg/day (300 mg/day if geriatric)* |
| clomipramine* (Anafranil®) | 12.5 to 150 mg/day PO QD | *250 mg/day (200 mg/day if pediatric)* |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| desipramine (Norpramin®) | 25 to 300 mg/day PO QD | *300 mg/day (100 mg/day if pediatric)* |
| doxepin (Sinequan®) | 25 to 300 mg/day PO QD | *300 mg/day* |
| imipramine HCl (Tofranil®) | 25 to 200 mg/day PO QD or divided doses | *200 mg/day (150 mg/day if geriatric or pediatric)* |
| imipramine pamoate (Tofranil PM®) | 25 to 200 mg/day PO QD or divided doses | *200 mg/day (100 mg/day if geriatric or pediatric)* |
| nortriptyline (Pamelor®) | 25 to 150 mg/day PO QD | *150 mg/day* |
| protriptyline (Vivactil®) | 10 to 60 mg/day PO in divided doses | *60 mg/day (30 mg/day if geriatric or pediatric)* |
| trimipramine (Surmontil®) | 25 to 200 mg/day PO QD | *200 mg/day (100 mg/day if geriatric or pediatric)* |
| ***Other Antidepressants*** | | |
| *bupropion (Aplenzin®, Budeprion SR® , Budeprion XL®, Forfivo XL®, Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)* | Varies | *Immediate-release: 450 mg/day (300 mg/day if pediatric)*<br>*Sustained-release: 400 mg/day*<br>*Extended-release (HCl): 450 mg/day*<br>*Extended-release (HBr): 522 mg/day* |
| *mirtazapine (Remeron®)* | 15 to 15 mg PO QD | *45 mg/day* |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Boxed warning(s): Excessive sedation and sudden loss of consciousness during administration. Patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Because of these risks, Zulresso is available only through a restricted program under a REMS program.
- Contraindication(s): none reported

*Appendix D: General Information*

- HAM-D scale is a 17-item depression assessment scale to assess severity of, and change in, depressive symptoms.

| HAM-D Score | Depression Rating |
|---|---|
| 0 – 7 | Normal, absence or remission of depression |
| 8 – 16 | Mild depression |
| 17 – 23 | Moderate depression |
| > 24 | Severe depression |

- MADRS is a 10-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders. Please note that MADRS severity gradations vary by reference. The following severity gradations are suggestions based on the reference cited below, and may not be universally agreed upon.

| MADRS Score | Depression Rating |
|---|---|
| 0 – 6 | Normal/symptom absent |
| 7 – 19 | Mild depression |
| 20 – 34 | Moderate depression |
| > 34 | Severe depression |

- PHQ-9 is a 9-item multiple choice questionnaire used for diagnosis, screening, monitoring and measuring the severity of depression.

| PHQ-9 Score | Depression Severity |
|---|---|
| 5 – 9 | Minimal symptoms |
| 10 – 14 | Minor depression<br>Major depression, mild |
| 15 – 19 | Major depression, moderately severe |
| > 20 | Major depression, severe |

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| PPD | Administered as a continuous intravenous infusion over 60 hours (2.5 days) as follows:<br>• 0 to 4 hours: Initiate with a dosage of 30 mcg/kg per hour<br>• 4 to 24 hours: Increase dosage to 60 mcg/kg per hour<br>• 24 to 52 hours: Increase dosage to 90 mcg/kg per hour (alternatively consider a dosage of 60 mcg/kg per hour for those who do not tolerate 90 mcg/kg per hour)<br>• 52 to 56 hours: Decrease dosage to 60 mcg/kg per hour<br>• 56 to 60 hours: Decrease dosage to 30 mcg/kg per hour | 90 mcg/kg per hour |

## VI. Product Availability

Vial for injection, single-dose: 100 mg/20 mL (5 mg/mL)

## VII. References

1. Zulresso Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc.; June 2022. Available at: www.zulresso.com. Accessed July 18, 2022.
2. Meltzer-Brody S, Colquhoun H, Riesenberg R, et al. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet. 2018 Sep 22;392(10152):1058-1070.
3. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline [CG192]. Available at: https://www.nice.org.uk/guidance/cg192. Accessed April 2, 2019.
4. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder, third edition. November 2010. Available at: http://psychiatryonline.org/guidelines.aspx. Accessed February 6, 2022.
5. Sharp, Rachel. The Hamilton rating scale for depression. Occupational Medicine. 2015; 65(4):340
6. Montgomery–Åsberg Depression Rating Scale. Available at: http://www.liquisearch.com/montgomery%E2%80%93%C3%85sberg_depression_rating_scale/interpretation. Accessed February 6, 2022.
7. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606–613.

## Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| C9055, J1632 | Injection, brexanolone, 1 mg |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 01/15/2020 | |
| 1Q 2020 annual review: added prescriber requirement; revised diagnosis with DSM-V definition of postpartum depression; revised criteria to allow bypass of 8-week antidepressant trial if member has severe depression as evidenced by HAMD, MADRS, or PHQ-9 score; updated HAM-D scale; references reviewed and updated. | 01/2021 | |
| 2Q 2021 annual review: no significant changes; references reviewed and updated. | 04/2021 | |
| 2Q 2022 annual review: references reviewed and updated. | 04/2022 | |
| RT4: per updated prescribing information, updated indication and age requirements from adults (18 years) to 15 years of age or older. | 08/2022 | |